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     FILE 'CAPLUS' ENTERED AT 14:40:27 ON 22 APR 2008
L1            24 S CLOPIDOGREL(L)(FORM(W)I)

=> s l1 and acetate
         560711 ACETATE
L2            11 L1 AND ACETATE

=> d bib hit 1-11

L2   ANSWER 1 OF 11  CAPLUS  COPYRIGHT 2008 ACS on STN
AN   2008:191638  CAPLUS
DN   148:246650
TI   Process for preparing clopidogrel bisulfate
IN   Singer, Claude; Masarwa, Basem; Sterimbaum, Greta; Daverio, Paola;
     Turgeman, Eran
PA   Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA,
     Inc.
SO   PCT Int. Appl., 15pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    -------------------    --------
PI   WO 2008019053       A2     20080214    WO 2007-US17324        20070803
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA,
             CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI,
             GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG,
             KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME,
             MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL,
             PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN,
             TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW,
             GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM
PRAI US 2006-835551P     P      20060803
     US 2006-858127P     P      20061109
     US 2006-877987P     P      20061228
AB   The invention relates to improved methods for the preparation of
     clopidogrel bisulfate, and especially for the preparation of the polymorphic
     Form I of clopidogrel bisulfate.  A process
     for preparing clopidogrel bisulfate Form I
     comprises (i) dissolving clopidogrel base in organic solvent
     selected from C4-5 ketones and C6-12 aromatic hydrocarbons to obtain a
solution,
     and (ii) adding sulfuric acid to the solution at 40° to obtain
     clopidogrel bisulfate Form I.
IT   64-18-6, Formic acid, uses   64-19-7, Acetic acid, uses   67-56-1,
     Methanol, uses   71-41-0, Pentanol, uses   108-10-1, Methyl isobutyl
     ketone   108-88-3, Toluene, uses   108-94-1, Cyclohexanone, uses
     141-78-6, Ethyl acetate, uses   151-21-3, Sodium lauryl sulfate,
     uses   1634-04-4
     RL: NUU (Other use, unclassified); USES (Uses)
        (process for preparing polymorphic form of clopidogrel bisulfate)

L2   ANSWER 2 OF 11  CAPLUS  COPYRIGHT 2008 ACS on STN
AN   2007:1028690  CAPLUS
DN   147:350539
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TI A process for the preparation of polymorph form I of (S)-(+)-clopidogrel hydrogen sulfate)
IN Garadnay, Sandor; Greiner, Istvan; Neu, Jozsef
PA Richter Gedeon Vegyeszeti Gyar Rt., Hung.
SO PCT Int. Appl., 36pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2007102037	A2	20070913	WO 2007-HU21	20070308
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	HU 2006000194	A2	20070928	HU 2006-194	20060309
	HU 2006000194	A3	20071228		
PRAI	HU 2006-194	A	20060309		

TI A process for the preparation of polymorph form I of (S)-(+)-clopidogrel hydrogen sulfate)

AB The invention relates to a process for the preparation of the pharmaceutically applicable polymorph form I of (S)-(+)-methyl-α-(2-chlorophenyl)-6,7-dihydro-thieno[3,2-c]-pyridine-5(4H)-acetate hydrogen sulfate ((S)-(+)-clopidogrel hydrogen sulfate) of formula I; by reacting (S)-(+)-methyl-α-(2-chlorophenyl)-6,7-dihydro-thieno[3,2-c]pyridine-5(4H)-acetate and sulfuric acid in the presence of solvents which comprises dissolving (S)-(+)-methyl-α-(2-chloropnenyl)-6,7-dihydro-thieno[3,2-c]pyridine-5(4H)-acetate in an ether; mixing this solution with a solution of a C6-C11 alc. and sulfuric acid; and recovering the so obtained compound of formula I from the mother liquor. Polymorph form I of ((S)-(+)-clopidogrel hydrogen sulfate) (I) was prepared by dissolving (S)-(+)-clopidogrel base in di-Et ether and stirring it with a mixture of sulfuric acid and 1-decanol for 48 h. The mixture was then filtered, washed and dried to obtain I having a m.p. of 184°-185°, yield = 84°.

IT Alcohols, uses
RL: NUU (Other use, unclassified); USES (Uses)
(C6-11; process for preparation of polymorph form I of (S)-(+)-clopidogrel hydrogen sulfate))

IT Ethers, uses
RL: NUU (Other use, unclassified); USES (Uses)
(aliphatic; process for preparation of polymorph form I of (S)-(+)-clopidogrel hydrogen sulfate))

IT Alcohols, uses
RL: NUU (Other use, unclassified); USES (Uses)
(primary; process for preparation of polymorph form I of (S)-(+)-clopidogrel hydrogen sulfate))

IT Polymorphism (crystal)
(process for preparation of polymorph form I of (S)-(+)-clopidogrel hydrogen sulfate))

IT Cycloalkanols

RL: NUU (Other use, unclassified); USES (Uses)
(process for preparation of polymorph form I of (S)-(+)-clopidogrel hydrogen sulfate))

IT Alcohols, uses
RL: NUU (Other use, unclassified); USES (Uses)
(secondary; process for preparation of polymorph form I of (S)-(+)-clopidogrel hydrogen sulfate))

IT Alcohols, uses
RL: NUU (Other use, unclassified); USES (Uses)
(tertiary; process for preparation of polymorph form I of (S)-(+)-clopidogrel hydrogen sulfate))

IT 112-30-1, 1-Decanol 1634-04-4, Methyl-tert-butyl ether
RL: NUU (Other use, unclassified); USES (Uses)
(process for preparation of polymorph form I of (S)-(+)-clopidogrel hydrogen sulfate))

IT 7664-93-9, Sulfuric acid, reactions 113665-84-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for preparation of polymorph form I of (S)-(+)-clopidogrel hydrogen sulfate))

IT 120202-66-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(process for preparation of polymorph form I of (S)-(+)-clopidogrel hydrogen sulfate))

L2 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2007:174397 CAPLUS
DN 146:213027
TI Novel process for preparation of clopidogrel bisulfate polymorphic Form I
IN Kamath, Ajit; Mali, Subhash; Ranbhan, Kamlesh; Patil, Jotiba; Zunjarrao, Yuvraj
PA Arch Pharmalabs Limited, India
SO PCT Int. Appl., 13pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007017886	A1	20070215	WO 2005-IN287	20050811

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI WO 2005-IN287 20050811
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Novel process for preparation of clopidogrel bisulfate polymorphic Form I
AB Disclosed herein is an efficient and cost-effective process for preparation of stable (S)-(+)-clopidogrel polymorphic Form I without affecting the chiral purity by dissolving/suspending the (S)-(+)-clopidogrel bisulfate Form II in first organic solvent and precipitating

using second organic solvent. The process is carried out at room temperature resulting in good yields and high purity. For example, 100 g of (S)-(+)-clopidogrel bisulfate Form II was dissolved in 400 mL of methanol at room temperature, methanol was distilled, the residue obtained was seeded with 2.2 g of (S)-(+)-clopidogrel bisulfate Form I and allowed to stir for 1 h. N-Bu acetate (800 mL) was added at room temperature to precipitate the solid. The solid was filtered, washed with Bu acetate and dried at room temperature to give 96.0 g of (S)-(+)-clopidogrel bisulfate Form I.

IT Alcohols, uses
RL: NUU (Other use, unclassified); USES (Uses)
(C1-3; organic solvents in preparation of clopidogrel bisulfate polymorphic Form I)

IT Crystal morphology
Polymorphism (crystal)
Precipitation (chemical)
(organic solvents in preparation of clopidogrel bisulfate polymorphic Form I)

IT Solvents
(organic; organic solvents in preparation of clopidogrel bisulfate polymorphic Form I)

IT 64-17-5, Ethanol, uses 64-19-7D, Acetic acid, C1-4 alkyl esters 67-56-1, Methanol, uses 67-63-0, Isopropanol, uses 79-20-9, Methyl acetate 123-86-4, n-Butyl acetate 141-78-6, Ethyl acetate, uses 540-88-5, tert-Butyl acetate
RL: NUU (Other use, unclassified); USES (Uses)
(organic solvents in preparation of clopidogrel bisulfate polymorphic Form I)

IT 120202-66-6, Clopidogrel bisulfate
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(organic solvents in preparation of clopidogrel bisulfate polymorphic Form I)

L2 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2007:101202 CAPLUS
DN 148:285078
TI Synthesis of crystalline forms I of clopidogrel hydrogen sulfate and mutual conversion of the crystalline forms
AU Pan, Xianhua; Mao, Haifang; Lang, Xihong
CS School of Biotechnology and Food Processing Engineering, Shanghai Institute of Technology, Shanghai, 200235, Peop. Rep. China
SO Jingxi Huagong (2006), 23(12), 1221-1226
CODEN: JIHUFJ; ISSN: 1003-5214
PB Jingxi Huagong Bianjibu
DT Journal
LA Chinese
AB A synthetic method for the production of crystalline form I of clopidogrel hydrogen sulfate (I) was improved. With 3-pentanone as solvent, a reaction at -10 to -16° for 10-16 h, gave I in 80% yield. A method for the mutual conversion of the crystalline form I and crystalline form II of clopidogrel (II) was also developed. I and II were characterized by m.p., FTIR spectrometry and x-ray powder diffraction.

IT 40412-06-4, 2-Thiopheneethanol 2-(4-methylbenzenesulfonate) 213018-92-9, (+)-(S)-Methyl α-amino-α-(2-chlorophenyl) acetate hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of crystalline forms I and II of clopidogrel hydrogen sulfate and

mutual conversion of crystalline forms)

IT 113665-84-2P, Clopidogrel 120202-66-6DP, Clopidogrel hydrogen sulfate, crystalline form I 120202-66-6DP, Clopidogrel hydrogen sulfate, crystalline form II 141109-19-5P, (+)-(S)-Methyl α-[[2-(2-thienyl)ethyl]amino]-α-(2-chlorophenyl) acetate hydrochloride
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of crystalline forms I and II of clopidogrel hydrogen sulfate and mutual conversion of crystalline forms)

L2 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:295243 CAPLUS
DN 144:338297
TI Crystalline clopidogrel hydrobromide and processes for preparation thereof
IN Finkelstein, Nina; Aronhime, Judith; Tessler, Limor
PA Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006034451	A2	20060330	WO 2005-US34149	20050921
	WO 2006034451	A3	20060810		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	US 20060154957	A1	20060713	US 2005-233491	20050921
	EP 1704152	A2	20060927	EP 2005-798184	20050921
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU				
	JP 2007513889	T	20070531	JP 2006-541522	20050921
	IN 2007DN01128	A	20070427	IN 2007-DN1128	20070212
	KR 2007052780	A	20070522	KR 2007-705407	20070307
PRAI	US 2004-611995P	P	20040921		
	US 2004-615771P	P	20041004		
	WO 2005-US34149	W	20050921		

AB Crystalline forms of clopidogrel hydrobromide for dosage forms and processes for their preparation are described. For example, a solution of 1.0 g (+)-clopidogrel in 90 mL of Et acetate was vigorously stirred with 48% aqueous hydrobromic acid (3.6 mL) at room temperature overnight., the solid was filtered, washed and dried to give 10.2 g (79%) of (+)-clopidogrel hydrobromide Form I.

IT 64-17-5, Ethanol, uses 67-63-0, Isopropanol, uses 67-64-1, Acetone, uses 71-23-8, n-Propanol, uses 75-65-0, tert-Butanol, uses 78-92-2, 2-Butanol 79-20-9, Methyl acetate 108-90-7, Chlorobenzene,

uses 109-99-9, Tetrahydrofuran, uses 123-91-1, Dioxane, uses 141-78-6, Ethyl acetate, uses 142-82-5, Heptane, uses 616-38-6, Dimethyl carbonate 1320-67-8, Propylene glycol methyl ether 25321-22-6, Dichlorobenzene
RL: NUU (Other use, unclassified); USES (Uses)
(preparation of crystalline clopidogrel hydrobromide for dosage forms)

L2 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:1154559 CAPLUS
DN 143:427350
TI Preparation of clopidogrel hydrogen sulfate polymorphic form I
IN Mao, Haifang; Qian, Hongguang; Chen, Chen
PA Krka, Tovarna Zdravil D.D. Novo Mesto, Slovenia
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005100364	A1	20051027	WO 2005-EP4160	20050419
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	SI 21749	A	20051031	SI 2004-122	20040421
	EP 1740593	A1	20070110	EP 2005-734224	20050419
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
	NO 2006005321	A	20070109	NO 2006-5321	20061120
PRAI	CN 2004-2004	A	20040419		
	SI 2004-122	A	20040421		
	CN 2004-10009028	A	20040419		
	WO 2005-EP4160	W	20050419		

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Preparation of clopidogrel hydrogen sulfate polymorphic form I
AB Processes for the preparation of clopidogrel (I) hydrogen sulfate of polymorphic form I are described which include use of specific solvents and process measures to avoid formation of undesired byproducts. I-HCl or a crystalline mixture of I H sulfate or I camphor sulfate is neutralized with a base such as K2CO3 to give I base and then an organic solvent solution treatment with concn H2SO4.
IT Crystal morphology
Polymorphism (crystal)
(preparation of clopidogrel hydrogen sulfate polymorphic form I)
IT 60-29-7, Diethyl ether, processes 67-66-3, Chloroform, processes 75-09-2, Dichloromethane, processes 79-20-9, Methyl acetate 108-20-3, Isopropyl ether 109-94-4, Ethyl formate 141-78-6, Ethyl

acetate, processes 1634-04-4, tert-Butyl methyl ether 7440-37-1, Argon, processes 7727-37-9, Nitrogen, processes RL: PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process)
(preparation of clopidogrel hydrogen sulfate polymorphic form I)

IT 120202-66-6P, Clopidogrel hydrogen sulfate
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of clopidogrel hydrogen sulfate polymorphic form I)

IT 584-08-7, Potassium carbonate 7664-93-9, Sulfuric acid, reactions 120202-65-5, Clopidogrel hydrochloride 120202-68-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of clopidogrel hydrogen sulfate polymorphic form I)

IT 113665-84-2P, Clopidogrel
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of clopidogrel hydrogen sulfate polymorphic form I)

L2 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:120929 CAPLUS
DN 142:204623
TI A novel process for the manufacture of (+)-(s)-clopidogrel bisulfate form-I
IN Jaweed Mukarram, Siddiqui Mohammed; Merwade, Aravind Yekanathsa; Khan, Anjum Reyaz
PA Wockhardt Limited, India
SO PCT Int. Appl., 9 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005012300	A1	20050210	WO 2003-IB3104	20030804
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2534893	A1	20050210	CA 2003-2534893	20030804
	AU 2003253120	A1	20050215	AU 2003-253120	20030804
	EP 1651646	A1	20060503	EP 2003-817742	20030804
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, SK				
	BR 2003018449	A	20060801	BR 2003-18449	20030804
	JP 2007516934	T	20070628	JP 2005-507351	20030804
	IN 2006MN00088	A	20060929	IN 2006-MN88	20060124
	US 20060183907	A1	20060817	US 2006-564364	20060223
	US 7291735	B2	20071106		
	US 20080051581	A1	20080228	US 2007-896853	20070906
PRAI	WO 2003-IB3104	W	20030804		
	US 2006-564364	A3	20060223		

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI A novel process for the manufacture of (+)-(s)-clopidogrel bisulfate form-I

AB The present invention relates to a novel process for the manufacture of blood-platelet aggregation inhibiting agent. In particular, the present invention is directed to a process for the manufacture of methyl-(+)-(S)-α-(2-chlorophenyl)-6,7-dihydrothieno[3,2-c]pyridine-S-(4H) acetate bisulfate Form-I. A solution of 4.50 gm (+)-(S)-clopidogrel in 50 mL Et acetate was seeded with (+)-(S)-clopidogrel bisulfate Form-I (2.5 % of the weight of base). During stirring 1.50 gm concentrate sulfuric acid was added at room temperature and the reaction slurry was heated at reflux for 1 h. Then it was stirred at room temperature for 1 h, the product was then filtered under suction and washed with Et acetate followed by drying under vacuum at 60° to 70° for 6-8 h. After complete drying, 4.0 gm (+)-(S)-clopidogrel bisulfate Form-I was obtained having 99.96 % purity.

IT Particle size
Polymorphism (crystal)
Solvents
(novel process for manufacture of clopidogrel bisulfate form-I)

IT 141-78-6, Ethyl acetate, uses
RL: NUU (Other use, unclassified); USES (Uses)
(novel process for manufacture of clopidogrel bisulfate form-I)

IT 7664-93-9, Sulfuric acid, reactions 35963-20-3 113665-84-2, (+)-(S)-Clopidogrel
RL: RCT (Reactant); RACT (Reactant or reagent)
(novel process for manufacture of clopidogrel bisulfate form-I)

IT 120202-66-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(novel process for manufacture of clopidogrel bisulfate form-I)

L2 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:470987 CAPLUS
DN 141:42905
TI Crystallization process for the preparation of the crystalline polymorphic form I of clopidogrel bisulfate
IN Piechaczek, Janina; Serafin, Jadwiga; Maruszak, Wioleta; Balicki, Roman; Szelejewski, Wieslaw; Cybulski, Marcin; Maciejewski, Grzegorz; Wysoczynska, Maria; Glice, Magdalena; Korczak, Katarzyna
PA Anpharm Przedsiebiorstwo Farmaceutyczne S.A., Pol.; et al.
SO PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004048385	A2	20040610	WO 2003-PL130	20031126
	WO 2004048385	A3	20040805		
	W: AL, AM, AT, AU, AZ, BA, BG, BR, BY, CA, CH, CN, CO, CZ, DE, DK, DM, EC, EE, ES, FI, GB, GD, GE, HR, HU, IL, IS, JP, KG, KR, KZ, LT, LU, LV, MA, MD, MK, MN, MW, MX, NI, NO, NZ, PT, RO, RU, SE,				

SK, SY, TJ, TM, TR, UA, US, UZ, YU, ZA
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR

AU 2003285841 A1 20040618 AU 2003-285841 20031126
PRAI PL 2002-254427 A 20021128
WO 2003-PL130 W 20031126

TI Crystallization process for the preparation of the crystalline polymorphic form I of clopidogrel bisulfate

AB The crystalline polymorphic form I of clopidogrel bisulfate is prepared by precipitating the salt formed in the neutralization reaction of the optically active base of clopidogrel, Me (S)-(+)-α-(2-chlorophenyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-5-acetate with concentrated sulfuric acid, using a precipitating solvent selected from aliphatic and cyclic ethers and iso-Bu Me ketone. An X-ray diffraction pattern of the title polymorphic compound is presented.

IT Crystallization
Polymorphism (crystal)
Precipitation (chemical)
(crystallization process for the preparation of the crystalline polymorphic form I of clopidogrel bisulfate)

IT Ethers, uses
RL: NUU (Other use, unclassified); REM (Removal or disposal); PROC (Process); USES (Uses)
(cyclic, solvents; in a crystallization process for the preparation of the crystalline polymorphic form I of clopidogrel bisulfate)

IT Neutralization
(of the free base with sulfuric acid in a crystallization process for the preparation of the crystalline polymorphic form I of clopidogrel bisulfate)

IT Ethers, uses
RL: NUU (Other use, unclassified); REM (Removal or disposal); PROC (Process); USES (Uses)
(solvents; in a crystallization process for the preparation of the crystalline polymorphic form I of clopidogrel bisulfate)

IT 120202-66-6P, Clopidogrel bisulfate
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(crystallization process for the preparation of the crystalline polymorphic form I of clopidogrel bisulfate)

IT 7664-93-9, Sulfuric acid, reactions 113665-84-2, Clopidogrel
RL: RCT (Reactant); RACT (Reactant or reagent)
(in a crystallization process for the preparation of the crystalline polymorphic form I of clopidogrel bisulfate)

IT 108-10-1, Methyl isobutyl ketone 110-71-4, 1,2-Dimethoxyethane 112-36-7, Bis(2-ethoxyethyl) ether 123-91-1, Dioxane, uses 629-14-1, 1,2-Diethoxyethane 1634-04-4, MTBE
RL: NUU (Other use, unclassified); REM (Removal or disposal); PROC (Process); USES (Uses)
(solvent; in a crystallization process for the preparation of the crystalline polymorphic form I of clopidogrel bisulfate)

L2 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:203837 CAPLUS

DN 140:241063
TI Method for the manufacture of crystalline form I of clopidogrel hydrogen sulfate
IN Veverka, Miroslav; Vodny, Stefan; Veverkova, Eva; Hajicek, Josef; Stepankova, Hana
PA Leciva, A.S., Czech Rep.
SO PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004020443	A1	20040311	WO 2003-CZ49	20030826
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CZ 297472	B6	20061213	CZ 2002-2906	20020827
	CA 2495823	A1	20040311	CA 2003-2495823	20030826
	AU 2003269673	A1	20040319	AU 2003-269673	20030826
	EP 1554284	A1	20050720	EP 2003-750270	20030826
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	JP 2006502238	T	20060119	JP 2004-569700	20030826
	US 20060041136	A1	20060223	US 2005-525341	20050706
PRAI	CZ 2002-2906	A	20020827		
	WO 2003-CZ49	W	20030826		

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Method for the manufacture of crystalline form I of clopidogrel hydrogen sulfate

AB A method for manufacturing the hydrogen sulfate (alpha S) of the alpha-(2-chlorophenyl)-6,7-dihydrothieno[3,2-c]pyridine-5(4H)-acetic acid Me ester (i.e., clopidogrel hydrogen sulfate), in crystalline Form I, where the compound is separated out of a solution of clopidogrel in the form of the free base or salt in a solvent selected from the series of primary, secondary or tertiary C1-5 alcs. (e.g., 2-propanol), their esters with C1-4 carboxylic acids, or optionally of mixts. thereof.

IT Carboxylic acids, uses
RL: NUU (Other use, unclassified); USES (Uses)
(esters, solvents; method for the manufacture of crystalline form I of clopidogrel hydrogen sulfate using)

IT Crystallization
Precipitation (chemical)
(method for the manufacture of crystalline form I of clopidogrel hydrogen sulfate using)

IT Alcohols, uses
RL: NUU (Other use, unclassified); USES (Uses)
(primary, C1-5, solvents; method for the manufacture of crystalline form I of clopidogrel hydrogen sulfate using)

IT Alcohols, uses
RL: NUU (Other use, unclassified); USES (Uses)
(secondary, solvents; method for the manufacture of crystalline form

I of clopidogrel hydrogen sulfate using)

IT Alcohols, uses
RL: NUU (Other use, unclassified); USES (Uses)
(tertiary, solvents; method for the manufacture of crystalline form I of clopidogrel hydrogen sulfate using)

IT 120202-66-6P, Clopidogrel hydrogen sulfate
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(method for the manufacture of crystalline form I of clopidogrel hydrogen sulfate)

IT 7664-93-9, Sulfuric acid, reactions 113665-84-2, Clopidogrel
RL: RCT (Reactant); RACT (Reactant or reagent)
(method for the manufacture of crystalline form I of clopidogrel hydrogen sulfate using)

IT 67-63-0, 2-Propanol, uses 141-78-6, Ethyl acetate, uses
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; method for the manufacture of crystalline form I of clopidogrel hydrogen sulfate using)

L2 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:491043 CAPLUS
DN 139:74015
TI Polymorphs of clopidogrel hydrogen sulfate
IN Lifshitz-Liron, Revital; Kovalevski-Ishai, Eti; Wizel, Shlomit; Avhar-Maydan, Sharon; Lidor-Hadas, Rami
PA Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SO PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003051362	A2	20030626	WO 2002-US40679	20021218
WO 2003051362	A3	20030807		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 20030114479	A1	20030619	US 2002-74409	20020212
US 6767913	B2	20040727		
CA 2470479	A1	20030626	CA 2002-2470479	20021218
AU 2002366383	A1	20030630	AU 2002-366383	20021218
AU 2002366383	B2	20070614		
EP 1467735	A2	20041020	EP 2002-805215	20021218
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
HU 2004002485	A2	20050428	HU 2004-2485	20021218
JP 2005514387	T	20050519	JP 2003-552295	20021218
US 20030225129	A1	20031204	US 2003-339008	20030108
US 7074928	B2	20060711		
ZA 2004004733	A	20050615	ZA 2004-4733	20040615
IN 2004DN01705	A	20070323	IN 2004-DN1705	20040616

	MX 2004PA06088	A	20040927	MX 2004-PA6088	20040617
	NO 2004003038	A	20040909	NO 2004-3038	20040716
	IN 2007DN08318	A	20080111	IN 2007-DN8318	20071029
PRAI	US 2001-342440P	P	20011218		
	US 2001-342351P	P	20011221		
	US 2002-348182P	P	20020111		
	US 2002-74409	A	20020212		
	US 2002-359157P	P	20020221		
	WO 2002-US40679	W	20021218		
	IN 2004-DN1705	A3	20040616		

AB Provided are new crystalline Forms III, IV, V and VI of clopidogrel hydrogen sulfate and the amorphous form of clopidogrel hydrogen sulfate, as well as their pharmaceutical compns. for inhibiting platelet aggregation. Also provided are novel processes for preparation of clopidogrel hydrogen sulfate Form I, Form II, Form III, Form IV, Form V, Form VI and amorphous form. For example, 5.31 g of clopidogrel base was dissolved in 41.9 mL of Et acetate, and 1.29 mL of 80% aqueous H_2SO_4 was added. The reaction mixture was heated and a massive precipitate was formed; the solution was cooled to room temperature, and white solid was collected by filtration, washed with Et acetate and dried to obtain 4.60 g (66%) clopidogrel hydrogen sulfate Form II.

IT 60-29-7, Diethyl ether, uses 64-17-5, Ethanol, uses 67-56-1, Methanol, uses 67-63-0, Isopropanol, uses 67-66-3, Chloroform, uses 71-23-8, 1-Propanol, uses 71-36-3, 1-Butanol, uses 75-05-8, Acetonitrile, uses 75-09-2, Dichloromethane, uses 78-92-2, 2-Butanol 78-93-3, Methyl ethyl ketone, uses 123-91-1, 1,4-Dioxane, uses 141-78-6, Ethyl acetate, uses 1634-04-4, Methyl tertbutyl ether
RL: NUU (Other use, unclassified); USES (Uses)
(preparation of amorphous and polymorphic forms of clopidogrel hydrogen sulfate for inhibition of platelet aggregation)

L2 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:473265 CAPLUS
DN 139:41853
TI preparation of crystal and amorphous forms of clopidogrel hydrogen sulfate for pharmaceuticals
IN Lifshitz-Liron, Revital; Kovalevski-Ishai, Eti; Wizel, Shlomit; Maydan, Sharon Avhar; Lidor-Hadas, Rami
PA Teva Pharmaceutical Industries Ltd., Israel
SO U.S. Pat. Appl. Publ., 27 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 20030114479	A1	20030619	US 2002-74409	20020212
	US 6767913	B2	20040727		
	CA 2470479	A1	20030626	CA 2002-2470479	20021218
	WO 2003051362	A2	20030626	WO 2002-US40679	20021218
	WO 2003051362	A3	20030807		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,

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             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     AU 2002366383          A1    20030630    AU 2002-366383          20021218
     AU 2002366383          B2    20070614
     EP 1467735             A2    20041020    EP 2002-805215          20021218
          R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
     HU 2004002485          A2    20050428    HU 2004-2485            20021218
     JP 2005514387          T     20050519    JP 2003-552295          20021218
     CN 1620293             A     20050525    CN 2002-828204          20021218
     CN 1923835             A     20070307    CN 2006-10139532        20021218
     US 20030225129         A1    20031204    US 2003-339008          20030108
     US 7074928             B2    20060711
     ZA 2004004733          A     20050615    ZA 2004-4733            20040615
     MX 2004PA06088         A     20040927    MX 2004-PA6088          20040617
     NO 2004003038          A     20040909    NO 2004-3038            20040716
PRAI US 2001-342440P        P     20011218
     US 2001-342351P        P     20011221
     US 2002-348182P        P     20020111
     US 2002-74409          A     20020212
     US 2002-359157P        P     20020221
     CN 2002-828204         A3    20021218
     WO 2002-US40679        W     20021218
RE.CNT  26     THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
               ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB   The present invention provides new crystalline forms III, IV and V of
     clopidogrel hydrogen sulfate and the amorphous form of
     clopidogrel hydrogen sulfate, as well as their pharmaceutical
     compns., and method of treatments with such compns.  The present invention
     further provides a novel process where the amorphous form is converted to
     Form I by contacting Form I with an
     ether.  Clopidogrel hydrogen sulfate (2 g) was dissolved in MeOH
     (4 mL).  The resulting solution was added dropwise to di-Et ether (350 mL).
     The suspension was stirred at room temperature for 45 min.  The solid was
     filtered and dried at about 50° in a vacuum oven for 24 h to give
     1.12 g (56%) of clopidogrel hydrogen sulfate, which
     characterization data showed to be the amorphous form.
IT   60-29-7, Diethyl ether, uses   64-17-5, Ethanol, uses   67-56-1, Methanol,
     uses   67-63-0, Isopropanol, uses   67-64-1, Acetone, uses   67-66-3,
     Chloroform, uses   71-23-8, 1-Propanol, uses   71-36-3, 1-Butanol, uses
     71-43-2, Benzene, uses   75-05-8, Acetonitrile, uses   75-09-2,
     Dichloromethane, uses   78-92-2, 2-Butanol   78-93-3, Methyl ethyl ketone,
     uses   108-88-3, Toluene, uses   123-91-1, 1,4-Dioxane, uses   141-78-6,
     Ethyl acetate, uses   1330-20-7, Xylene, uses   1634-04-4,
     tert-Butyl methyl ether
     RL: NUU (Other use, unclassified); PEP (Physical, engineering or chemical
     process); PYP (Physical process); PROC (Process); USES (Uses)
        (preparation of crystal and amorphous forms of clopidogrel hydrogen sulfate
        for pharmaceuticals)


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     (FILE 'HOME' ENTERED AT 14:40:16 ON 22 APR 2008)

     FILE 'CAPLUS' ENTERED AT 14:40:27 ON 22 APR 2008
L1            24 S CLOPIDOGREL(L)(FORM(W)I)
L2            11 S L1 AND ACETATE

=> d bib hit 1-11
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L2 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2008:191638 CAPLUS
DN 148:246650
TI Process for preparing clopidogrel bisulfate
IN Singer, Claude; Masarwa, Basem; Sterimbaum, Greta; Daverio, Paola; Turgeman, Eran
PA Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SO PCT Int. Appl., 15pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2008019053	A2	20080214	WO 2007-US17324	20070803

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2006-835551P	P	20060803	
US 2006-858127P	P	20061109	
US 2006-877987P	P	20061228	

AB The invention relates to improved methods for the preparation of clopidogrel bisulfate, and especially for the preparation of the polymorphic Form I of clopidogrel bisulfate. A process for preparing clopidogrel bisulfate Form I comprises (i) dissolving clopidogrel base in organic solvent selected from C4-5 ketones and C6-12 aromatic hydrocarbons to obtain a solution, and (ii) adding sulfuric acid to the solution at 40° to obtain clopidogrel bisulfate Form I.
IT 64-18-6, Formic acid, uses 64-19-7, Acetic acid, uses 67-56-1, Methanol, uses 71-41-0, Pentanol, uses 108-10-1, Methyl isobutyl ketone 108-88-3, Toluene, uses 108-94-1, Cyclohexanone, uses 141-78-6, Ethyl acetate, uses 151-21-3, Sodium lauryl sulfate, uses 1634-04-4
RL: NUU (Other use, unclassified); USES (Uses)
(process for preparing polymorphic form of clopidogrel bisulfate)

L2 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2007:1028690 CAPLUS
DN 147:350539
TI A process for the preparation of polymorph form I of (S)-(+)-clopidogrel hydrogen sulfate)
IN Garadnay, Sandor; Greiner, Istvan; Neu, Jozsef
PA Richter Gedeon Vegyeszeti Gyar Rt., Hung.
SO PCT Int. Appl., 36pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI	WO 2007102037	A2	20070913	WO 2007-HU21	20070308
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	HU 2006000194	A2	20070928	HU 2006-194	20060309
	HU 2006000194	A3	20071228		
PRAI	HU 2006-194	A	20060309		

TI A process for the preparation of polymorph form I of (S)-(+)-clopidogrel hydrogen sulfate)

AB The invention relates to a process for the preparation of the pharmaceutically applicable polymorph form I of (S)-(+)-methyl-α-(2-chlorophenyl)-6,7-dihydro-thieno[3,2-c]-pyridine-5(4H)-acetate hydrogen sulfate ((S)-(+)-clopidogrel hydrogen sulfate) of formula I; by reacting (S)-(+)-methyl-α-(2-chlorophenyl)-6,7-dihydro-thieno[3,2-c]pyridine-5(4H)-acetate and sulfuric acid in the presence of solvents which comprises dissolving (S)-(+)-methyl-α-(2-chloropnenyl)-6,7-dihydro-thieno[3,2-c]pyridine-5(4H)-acetate in an ether; mixing this solution with a solution of a C6-C11 alc. and sulfuric acid; and recovering the so obtained compound of formula I from the mother liquor. Polymorph form I of ((S)-(+)-clopidogrel hydrogen sulfate) (I) was prepared by dissolving (S)-(+)-clopidogrel base in di-Et ether and stirring it with a mixture of sulfuric acid and 1-decanol for 48 h. The mixture was then filtered, washed and dried to obtain I having a m.p. of 184°-185°, yield = 84°.

IT Alcohols, uses
RL: NUU (Other use, unclassified); USES (Uses)
(C6-11; process for preparation of polymorph form I of (S)-(+)-clopidogrel hydrogen sulfate))

IT Ethers, uses
RL: NUU (Other use, unclassified); USES (Uses)
(aliphatic; process for preparation of polymorph form I of (S)-(+)-clopidogrel hydrogen sulfate))

IT Alcohols, uses
RL: NUU (Other use, unclassified); USES (Uses)
(primary; process for preparation of polymorph form I of (S)-(+)-clopidogrel hydrogen sulfate))

IT Polymorphism (crystal)
(process for preparation of polymorph form I of (S)-(+)-clopidogrel hydrogen sulfate))

IT Cycloalkanols
RL: NUU (Other use, unclassified); USES (Uses)
(process for preparation of polymorph form I of (S)-(+)-clopidogrel hydrogen sulfate))

IT Alcohols, uses
RL: NUU (Other use, unclassified); USES (Uses)
(secondary; process for preparation of polymorph form I of (S)-(+)-clopidogrel hydrogen sulfate))

IT Alcohols, uses
RL: NUU (Other use, unclassified); USES (Uses)
(tertiary; process for preparation of polymorph form I

of (S)-(+)-clopidogrel hydrogen sulfate))
IT 112-30-1, 1-Decanol 1634-04-4, Methyl-tert-butyl ether
RL: NUU (Other use, unclassified); USES (Uses)
(process for preparation of polymorph form I of (S)-(+)-clopidogrel hydrogen sulfate))
IT 7664-93-9, Sulfuric acid, reactions 113665-84-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for preparation of polymorph form I of (S)-(+)-clopidogrel hydrogen sulfate))
IT 120202-66-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(process for preparation of polymorph form I of (S)-(+)-clopidogrel hydrogen sulfate))

L2 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2007:174397 CAPLUS
DN 146:213027
TI Novel process for preparation of clopidogrel bisulfate polymorphic Form I
IN Kamath, Ajit; Mali, Subhash; Ranbhan, Kamlesh; Patil, Jotiba; Zunjarrao, Yuvraj
PA Arch Pharmalabs Limited, India
SO PCT Int. Appl., 13pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007017886	A1	20070215	WO 2005-IN287	20050811
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRAI WO 2005-IN287		20050811		

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Novel process for preparation of clopidogrel bisulfate polymorphic Form I
AB Disclosed herein is an efficient and cost-effective process for preparation of stable (S)-(+)-clopidogrel polymorphic Form I without affecting the chiral purity by dissolving/suspending the (S)-(+)-clopidogrel bisulfate Form II in first organic solvent and precipitating using second organic solvent. The process is carried out at room temperature resulting in good yields and high purity. For example, 100 g of (S)-(+)-clopidogrel bisulfate Form II was dissolved in 400 mL of methanol at room temperature, methanol was distilled, the residue obtained was seeded with 2.2 g of (S)-(+)-clopidogrel bisulfate Form I and allowed to stir for 1 h. N-Bu acetate (800 mL) was added at room temperature to precipitate the solid. The solid was filtered, washed with Bu acetate and dried at room temperature to give 96.0 g of (S)-(+)-

clopidogrel bisulfate Form I.

IT Alcohols, uses
RL: NUU (Other use, unclassified); USES (Uses)
(C1-3; organic solvents in preparation of clopidogrel bisulfate polymorphic Form I)

IT Crystal morphology
Polymorphism (crystal)
Precipitation (chemical)
(organic solvents in preparation of clopidogrel bisulfate polymorphic Form I)

IT Solvents
(organic; organic solvents in preparation of clopidogrel bisulfate polymorphic Form I)

IT 64-17-5, Ethanol, uses 64-19-7D, Acetic acid, C1-4 alkyl esters 67-56-1, Methanol, uses 67-63-0, Isopropanol, uses 79-20-9, Methyl acetate 123-86-4, n-Butyl acetate 141-78-6, Ethyl acetate, uses 540-88-5, tert-Butyl acetate
RL: NUU (Other use, unclassified); USES (Uses)
(organic solvents in preparation of clopidogrel bisulfate polymorphic Form I)

IT 120202-66-6, Clopidogrel bisulfate
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(organic solvents in preparation of clopidogrel bisulfate polymorphic Form I)

L2 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2007:101202 CAPLUS
DN 148:285078
TI Synthesis of crystalline forms I of clopidogrel hydrogen sulfate and mutual conversion of the crystalline forms
AU Pan, Xianhua; Mao, Haifang; Lang, Xihong
CS School of Biotechnology and Food Processing Engineering, Shanghai Institute of Technology, Shanghai, 200235, Peop. Rep. China
SO Jingxi Huagong (2006), 23(12), 1221-1226
CODEN: JIHUFJ; ISSN: 1003-5214
PB Jingxi Huagong Bianjibu
DT Journal
LA Chinese
AB A synthetic method for the production of crystalline form I of clopidogrel hydrogen sulfate (I) was improved. With 3-pentanone as solvent, a reaction at -10 to -16° for 10-16 h, gave I in 80% yield. A method for the mutual conversion of the crystalline form I and crystalline form II of clopidogrel (II) was also developed. I and II were characterized by m.p., FTIR spectrometry and x-ray powder diffraction.

IT 40412-06-4, 2-Thiopheneethanol 2-(4-methylbenzenesulfonate) 213018-92-9, (+)-(S)-Methyl α-amino-α-(2-chlorophenyl) acetate hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of crystalline forms I and II of clopidogrel hydrogen sulfate and mutual conversion of crystalline forms)

IT 113665-84-2P, Clopidogrel 120202-66-6DP, Clopidogrel hydrogen sulfate, crystalline form I 120202-66-6DP, Clopidogrel hydrogen sulfate, crystalline form II 141109-19-5P, (+)-(S)-Methyl α-[[2-(2-thienyl)ethyl]amino]-α-(2-chlorophenyl) acetate hydrochloride
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of crystalline forms I and II of clopidogrel hydrogen

sulfate and mutual conversion of crystalline forms)

L2 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:295243 CAPLUS
DN 144:338297
TI Crystalline clopidogrel hydrobromide and processes for preparation thereof
IN Finkelstein, Nina; Aronhime, Judith; Tessler, Limor
PA Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006034451	A2	20060330	WO 2005-US34149	20050921
	WO 2006034451	A3	20060810		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	US 20060154957	A1	20060713	US 2005-233491	20050921
	EP 1704152	A2	20060927	EP 2005-798184	20050921
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU				
	JP 2007513889	T	20070531	JP 2006-541522	20050921
	IN 2007DN01128	A	20070427	IN 2007-DN1128	20070212
	KR 2007052780	A	20070522	KR 2007-705407	20070307
PRAI	US 2004-611995P	P	20040921		
	US 2004-615771P	P	20041004		
	WO 2005-US34149	W	20050921		

AB Crystalline forms of clopidogrel hydrobromide for dosage forms and processes for their preparation are described. For example, a solution of 1.0 g (+)-clopidogrel in 90 mL of Et acetate was vigorously stirred with 48% aqueous hydrobromic acid (3.6 mL) at room temperature overnight., the solid was filtered, washed and dried to give 10.2 g (79%) of (+)-clopidogrel hydrobromide Form I.

IT 64-17-5, Ethanol, uses 67-63-0, Isopropanol, uses 67-64-1, Acetone, uses 71-23-8, n-Propanol, uses 75-65-0, tert-Butanol, uses 78-92-2, 2-Butanol 79-20-9, Methyl acetate 108-90-7, Chlorobenzene, uses 109-99-9, Tetrahydrofuran, uses 123-91-1, Dioxane, uses 141-78-6, Ethyl acetate, uses 142-82-5, Heptane, uses 616-38-6, Dimethyl carbonate 1320-67-8, Propylene glycol methyl ether 25321-22-6, Dichlorobenzene
RL: NUU (Other use, unclassified); USES (Uses)
(preparation of crystalline clopidogrel hydrobromide for dosage forms)

L2 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:1154559 CAPLUS

DN 143:427350
TI Preparation of clopidogrel hydrogen sulfate polymorphic form I
IN Mao, Haifang; Qian, Hongguang; Chen, Chen
PA Krka, Tovarna Zdravil D.D. Novo Mesto, Slovenia
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005100364	A1	20051027	WO 2005-EP4160	20050419
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	SI 21749	A	20051031	SI 2004-122	20040421
	EP 1740593	A1	20070110	EP 2005-734224	20050419
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
	NO 2006005321	A	20070109	NO 2006-5321	20061120
PRAI	CN 2004-2004	A	20040419		
	SI 2004-122	A	20040421		
	CN 2004-10009028	A	20040419		
	WO 2005-EP4160	W	20050419		

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Preparation of clopidogrel hydrogen sulfate polymorphic form I

AB Processes for the preparation of clopidogrel (I) hydrogen sulfate of polymorphic form I are described which include use of specific solvents and process measures to avoid formation of undesired byproducts. I-HCl or a crystalline mixture of I H sulfate or I camphor sulfate is neutralized with a base such as K2CO3 to give I base and then an organic solvent solution treatment with concn H2SO4.

IT Crystal morphology
Polymorphism (crystal)
(preparation of clopidogrel hydrogen sulfate polymorphic form I)

IT 60-29-7, Diethyl ether, processes 67-66-3, Chloroform, processes 75-09-2, Dichloromethane, processes 79-20-9, Methyl acetate 108-20-3, Isopropyl ether 109-94-4, Ethyl formate 141-78-6, Ethyl acetate, processes 1634-04-4, tert-Butyl methyl ether 7440-37-1, Argon, processes 7727-37-9, Nitrogen, processes
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process)
(preparation of clopidogrel hydrogen sulfate polymorphic form I)

IT 120202-66-6P, Clopidogrel hydrogen sulfate
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of clopidogrel hydrogen sulfate polymorphic form I)

IT 584-08-7, Potassium carbonate 7664-93-9, Sulfuric acid, reactions 120202-65-5, Clopidogrel hydrochloride 120202-68-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of clopidogrel hydrogen sulfate polymorphic form I)

IT 113665-84-2P, Clopidogrel
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of clopidogrel hydrogen sulfate polymorphic form I)

L2 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:120929 CAPLUS
DN 142:204623
TI A novel process for the manufacture of (+)-(s)-clopidogrel bisulfate form-I
IN Jaweed Mukarram, Siddiqui Mohammed; Merwade, Aravind Yekanathsa; Khan, Anjum Rayeq
PA Wockhardt Limited, India
SO PCT Int. Appl., 9 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005012300	A1	20050210	WO 2003-IB3104	20030804
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2534893	A1	20050210	CA 2003-2534893	20030804
	AU 2003253120	A1	20050215	AU 2003-253120	20030804
	EP 1651646	A1	20060503	EP 2003-817742	20030804
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, SK				
	BR 2003018449	A	20060801	BR 2003-18449	20030804
	JP 2007516934	T	20070628	JP 2005-507351	20030804
	IN 2006MN00088	A	20060929	IN 2006-MN88	20060124
	US 20060183907	A1	20060817	US 2006-564364	20060223
	US 7291735	B2	20071106		
	US 20080051581	A1	20080228	US 2007-896853	20070906
PRAI	WO 2003-IB3104	W	20030804		
	US 2006-564364	A3	20060223		

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI A novel process for the manufacture of (+)-(s)-clopidogrel bisulfate form-I
AB The present invention relates to a novel process for the manufacture of blood-platelet aggregation inhibiting agent. In particular, the present invention is directed to a process for the manufacture of methyl-(+)-(S)-α-(2-chlorophenyl)-6,7-dihydrothieno[3,2-c]pyridine-5-(4H) acetate bisulfate Form-I. A solution of 4.50 gm

(+)-(S)-clopidogrel in 50 mL Et acetate was seeded with (+)-(S)-clopidogrel bisulfate Form-I (2.5 % of the weight of base). During stirring 1.50 gm concentrate sulfuric acid was added at room temperature and the reaction slurry was heated at reflux for 1 h. Then it was stirred at room temperature for 1 h, the product was then filtered under suction and washed with Et acetate followed by drying under vacuum at 60° to 70° for 6-8 h. After complete drying, 4.0 gm (+)-(S)-clopidogrel bisulfate Form-I was obtained having 99.96 % purity.

IT Particle size
Polymorphism (crystal)
Solvents
(novel process for manufacture of clopidogrel bisulfate form-I)

IT 141-78-6, Ethyl acetate, uses
RL: NUU (Other use, unclassified); USES (Uses)
(novel process for manufacture of clopidogrel bisulfate form-I)

IT 7664-93-9, Sulfuric acid, reactions 35963-20-3 113665-84-2, (+)-(S)-Clopidogrel
RL: RCT (Reactant); RACT (Reactant or reagent)
(novel process for manufacture of clopidogrel bisulfate form-I)

IT 120202-66-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(novel process for manufacture of clopidogrel bisulfate form-I)

L2 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:470987 CAPLUS
DN 141:42905
TI Crystallization process for the preparation of the crystalline polymorphic form I of clopidogrel bisulfate
IN Piechaczek, Janina; Serafin, Jadwiga; Maruszak, Wioleta; Balicki, Roman; Szelejewski, Wieslaw; Cybulski, Marcin; Maciejewski, Grzegorz; Wysoczynska, Maria; Glice, Magdalena; Korczak, Katarzyna
PA Anpharm Przedsiebiorstwo Farmaceutyczne S.A., Pol.; et al.
SO PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004048385	A2	20040610	WO 2003-PL130	20031126
WO 2004048385	A3	20040805		
W: AL, AM, AT, AU, AZ, BA, BG, BR, BY, CA, CH, CN, CO, CZ, DE, DK, DM, EC, EE, ES, FI, GB, GD, GE, HR, HU, IL, IS, JP, KG, KR, KZ, LT, LU, LV, MA, MD, MK, MN, MW, MX, NI, NO, NZ, PT, RO, RU, SE, SK, SY, TJ, TM, TR, UA, US, UZ, YU, ZA				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
AU 2003285841	A1	20040618	AU 2003-285841	20031126
PRAI PL 2002-254427	A	20021128		
WO 2003-PL130	W	20031126		

TI Crystallization process for the preparation of the crystalline polymorphic form I of clopidogrel bisulfate

AB The crystalline polymorphic form I of clopidogrel bisulfate is prepared by precipitating the salt formed in the neutralization reaction of the optically active base of clopidogrel, Me (S)-(+)-α-(2-chlorophenyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-5-acetate with concentrated sulfuric acid, using a precipitating solvent selected from aliphatic and cyclic ethers and iso-Bu Me ketone. An X-ray diffraction pattern of the title polymorphic compound is presented.

IT Crystallization
Polymorphism (crystal)
Precipitation (chemical)
(crystallization process for the preparation of the crystalline polymorphic form I of clopidogrel bisulfate)

IT Ethers, uses
RL: NUU (Other use, unclassified); REM (Removal or disposal); PROC (Process); USES (Uses)
(cyclic, solvents; in a crystallization process for the preparation of the crystalline polymorphic form I of clopidogrel bisulfate)

IT Neutralization
(of the free base with sulfuric acid in a crystallization process for the preparation of the crystalline polymorphic form I of clopidogrel bisulfate)

IT Ethers, uses
RL: NUU (Other use, unclassified); REM (Removal or disposal); PROC (Process); USES (Uses)
(solvents; in a crystallization process for the preparation of the crystalline polymorphic form I of clopidogrel bisulfate)

IT 120202-66-6P, Clopidogrel bisulfate
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(crystallization process for the preparation of the crystalline polymorphic form I of clopidogrel bisulfate)

IT 7664-93-9, Sulfuric acid, reactions 113665-84-2, Clopidogrel
RL: RCT (Reactant); RACT (Reactant or reagent)
(in a crystallization process for the preparation of the crystalline polymorphic form I of clopidogrel bisulfate)

IT 108-10-1, Methyl isobutyl ketone 110-71-4, 1,2-Dimethoxyethane 112-36-7, Bis(2-ethoxyethyl) ether 123-91-1, Dioxane, uses 629-14-1, 1,2-Diethoxyethane 1634-04-4, MTBE
RL: NUU (Other use, unclassified); REM (Removal or disposal); PROC (Process); USES (Uses)
(solvent; in a crystallization process for the preparation of the crystalline polymorphic form I of clopidogrel bisulfate)

L2 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:203837 CAPLUS
DN 140:241063
TI Method for the manufacture of crystalline form I of clopidogrel hydrogen sulfate
IN Veverka, Miroslav; Vodny, Stefan; Veverkova, Eva; Hajicek, Josef; Stepankova, Hana
PA Leciva, A.S., Czech Rep.
SO PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DT Patent

LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004020443	A1	20040311	WO 2003-CZ49	20030826
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CZ 297472	B6	20061213	CZ 2002-2906	20020827
	CA 2495823	A1	20040311	CA 2003-2495823	20030826
	AU 2003269673	A1	20040319	AU 2003-269673	20030826
	EP 1554284	A1	20050720	EP 2003-750270	20030826
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	JP 2006502238	T	20060119	JP 2004-569700	20030826
	US 20060041136	A1	20060223	US 2005-525341	20050706
PRAI	CZ 2002-2906	A	20020827		
	WO 2003-CZ49	W	20030826		

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Method for the manufacture of crystalline form I of clopidogrel hydrogen sulfate

AB A method for manufacturing the hydrogen sulfate (alpha S) of the alpha-(2-chlorophenyl)-6,7-dihydrothieno[3,2-c]pyridine-5(4H)-acetic acid Me ester (i.e., clopidogrel hydrogen sulfate), in crystalline Form I, where the compound is separated out of a solution of clopidogrel in the form of the free base or salt in a solvent selected from the series of primary, secondary or tertiary C1-5 alcs. (e.g., 2-propanol), their esters with C1-4 carboxylic acids, or optionally of mixts. thereof.

IT Carboxylic acids, uses
RL: NUU (Other use, unclassified); USES (Uses)
(esters, solvents; method for the manufacture of crystalline form I of clopidogrel hydrogen sulfate using)

IT Crystallization
Precipitation (chemical)
(method for the manufacture of crystalline form I of clopidogrel hydrogen sulfate using)

IT Alcohols, uses
RL: NUU (Other use, unclassified); USES (Uses)
(primary, C1-5, solvents; method for the manufacture of crystalline form I of clopidogrel hydrogen sulfate using)

IT Alcohols, uses
RL: NUU (Other use, unclassified); USES (Uses)
(secondary, solvents; method for the manufacture of crystalline form I of clopidogrel hydrogen sulfate using)

IT Alcohols, uses
RL: NUU (Other use, unclassified); USES (Uses)
(tertiary, solvents; method for the manufacture of crystalline form I of clopidogrel hydrogen sulfate using)

IT 120202-66-6P, Clopidogrel hydrogen sulfate
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)

(method for the manufacture of crystalline form I of clopidogrel hydrogen sulfate)
IT 7664-93-9, Sulfuric acid, reactions 113665-84-2, Clopidogrel
RL: RCT (Reactant); RACT (Reactant or reagent)
(method for the manufacture of crystalline form I of clopidogrel hydrogen sulfate using)
IT 67-63-0, 2-Propanol, uses 141-78-6, Ethyl acetate, uses
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; method for the manufacture of crystalline form I of clopidogrel hydrogen sulfate using)

L2 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:491043 CAPLUS
DN 139:74015
TI Polymorphs of clopidogrel hydrogen sulfate
IN Lifshitz-Liron, Revital; Kovalevski-Ishai, Eti; Wizel, Shlomit; Avhar-Maydan, Sharon; Lidor-Hadas, Rami
PA Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SO PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003051362	A2	20030626	WO 2002-US40679	20021218
	WO 2003051362	A3	20030807		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 20030114479	A1	20030619	US 2002-74409	20020212
	US 6767913	B2	20040727		
	CA 2470479	A1	20030626	CA 2002-2470479	20021218
	AU 2002366383	A1	20030630	AU 2002-366383	20021218
	AU 2002366383	B2	20070614		
	EP 1467735	A2	20041020	EP 2002-805215	20021218
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
	HU 2004002485	A2	20050428	HU 2004-2485	20021218
	JP 2005514387	T	20050519	JP 2003-552295	20021218
	US 20030225129	A1	20031204	US 2003-339008	20030108
	US 7074928	B2	20060711		
	ZA 2004004733	A	20050615	ZA 2004-4733	20040615
	IN 2004DN01705	A	20070323	IN 2004-DN1705	20040616
	MX 2004PA06088	A	20040927	MX 2004-PA6088	20040617
	NO 2004003038	A	20040909	NO 2004-3038	20040716
	IN 2007DN08318	A	20080111	IN 2007-DN8318	20071029
PRAI	US 2001-342440P	P	20011218		
	US 2001-342351P	P	20011221		
	US 2002-348182P	P	20020111		
	US 2002-74409	A	20020212		
	US 2002-359157P	P	20020221		
	WO 2002-US40679	W	20021218		

IN 2004-DN1705 A3 20040616

AB Provided are new crystalline Forms III, IV, V and VI of clopidogrel hydrogen sulfate and the amorphous form of clopidogrel hydrogen sulfate, as well as their pharmaceutical compns. for inhibiting platelet aggregation. Also provided are novel processes for preparation of clopidogrel hydrogen sulfate Form I, Form II, Form III, Form IV, Form V, Form VI and amorphous form. For example, 5.31 g of clopidogrel base was dissolved in 41.9 mL of Et acetate, and 1.29 mL of 80% aqueous H2SO4 was added. The reaction mixture was heated and a massive precipitate was formed; the solution was cooled to room temperature, and white solid was collected by filtration, washed with Et acetate and dried to obtain 4.60 g (66%) clopidogrel hydrogen sulfate Form II.

IT 60-29-7, Diethyl ether, uses 64-17-5, Ethanol, uses 67-56-1, Methanol, uses 67-63-0, Isopropanol, uses 67-66-3, Chloroform, uses 71-23-8, 1-Propanol, uses 71-36-3, 1-Butanol, uses 75-05-8, Acetonitrile, uses 75-09-2, Dichloromethane, uses 78-92-2, 2-Butanol 78-93-3, Methyl ethyl ketone, uses 123-91-1, 1,4-Dioxane, uses 141-78-6, Ethyl acetate, uses 1634-04-4, Methyl tertbutyl ether
RL: NUU (Other use, unclassified); USES (Uses)
(preparation of amorphous and polymorphic forms of clopidogrel hydrogen sulfate for inhibition of platelet aggregation)

L2 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:473265 CAPLUS
DN 139:41853
TI preparation of crystal and amorphous forms of clopidogrel hydrogen sulfate for pharmaceuticals
IN Lifshitz-Liron, Revital; Kovalevski-Ishai, Eti; Wizel, Shlomit; Maydan, Sharon Avhar; Lidor-Hadas, Rami
PA Teva Pharmaceutical Industries Ltd., Israel
SO U.S. Pat. Appl. Publ., 27 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 20030114479	A1	20030619	US 2002-74409	20020212
	US 6767913	B2	20040727		
	CA 2470479	A1	20030626	CA 2002-2470479	20021218
	WO 2003051362	A2	20030626	WO 2002-US40679	20021218
	WO 2003051362	A3	20030807		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002366383	A1	20030630	AU 2002-366383	20021218
	AU 2002366383	B2	20070614		
	EP 1467735	A2	20041020	EP 2002-805215	20021218
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
	HU 2004002485	A2	20050428	HU 2004-2485	20021218
	JP 2005514387	T	20050519	JP 2003-552295	20021218

	CN 1620293	A	20050525	CN 2002-828204	20021218
	CN 1923835	A	20070307	CN 2006-10139532	20021218
	US 20030225129	A1	20031204	US 2003-339008	20030108
	US 7074928	B2	20060711		
	ZA 2004004733	A	20050615	ZA 2004-4733	20040615
	MX 2004PA06088	A	20040927	MX 2004-PA6088	20040617
	NO 2004003038	A	20040909	NO 2004-3038	20040716
PRAI	US 2001-342440P	P	20011218		
	US 2001-342351P	P	20011221		
	US 2002-348182P	P	20020111		
	US 2002-74409	A	20020212		
	US 2002-359157P	P	20020221		
	CN 2002-828204	A3	20021218		
	WO 2002-US40679	W	20021218		

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB The present invention provides new crystalline forms III, IV and V of clopidogrel hydrogen sulfate and the amorphous form of clopidogrel hydrogen sulfate, as well as their pharmaceutical compns., and method of treatments with such compns. The present invention further provides a novel process where the amorphous form is converted to Form I by contacting Form I with an ether. Clopidogrel hydrogen sulfate (2 g) was dissolved in MeOH (4 mL). The resulting solution was added dropwise to di-Et ether (350 mL). The suspension was stirred at room temperature for 45 min. The solid was filtered and dried at about 50° in a vacuum oven for 24 h to give 1.12 g (56%) of clopidogrel hydrogen sulfate, which characterization data showed to be the amorphous form.

IT 60-29-7, Diethyl ether, uses 64-17-5, Ethanol, uses 67-56-1, Methanol, uses 67-63-0, Isopropanol, uses 67-64-1, Acetone, uses 67-66-3, Chloroform, uses 71-23-8, 1-Propanol, uses 71-36-3, 1-Butanol, uses 71-43-2, Benzene, uses 75-05-8, Acetonitrile, uses 75-09-2, Dichloromethane, uses 78-92-2, 2-Butanol 78-93-3, Methyl ethyl ketone, uses 108-88-3, Toluene, uses 123-91-1, 1,4-Dioxane, uses 141-78-6, Ethyl acetate, uses 1330-20-7, Xylene, uses 1634-04-4, tert-Butyl methyl ether
RL: NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process); USES (Uses)
(preparation of crystal and amorphous forms of clopidogrel hydrogen sulfate for pharmaceuticals)